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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.: 09/821,726
Patent No.: 6,734,289
Invention: GASTROKINES AND DERIVED
PEPTIDES INCLUDING
INHIBITORS
Applicant: Terence Martin et al.
Filed: March 29, 2001
Attorney
Docket: 21459-90913
Examiner: Daniel M. Sullivan

Certificate Under 37 CFR 1.8(a)

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on March 9, 2007

Alice O. Martin
Alice O. Martin

COMMUNICATION

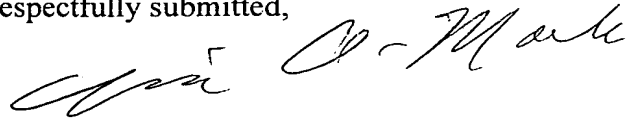
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Commissioner for Patents
P.O. Box 1450
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Sir:

Please enter in the file of the patent captioned above the attached "Amendment and Response to Examiner's Communication" which was filed by facsimile on December 1, 2003 with the U.S. Patent and Trademark Office. We note this paper does not appear in PAIR but as shown by the attached facsimile sheet to (703) 746-9105 was received at the U.S. Patent and Trademark Office. This is **not** a request for any certificate of correction.

No fees are believed due at this time, however, please charge any deficiencies or credit any overpayments to deposit account number 12-0913 with reference to our attorney docket number (21459-90913).

Respectfully submitted,

A handwritten signature in cursive script, appearing to read "Alice O. Martin".

Alice O. Martin
Reg. No. 35,601

Dated: March 9, 2007

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P. O. Box 2786
Chicago, IL 60690

* * * COMMUNICATION RESULT REPORT (DEC. 1. 2003 4:23PM) * * *

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Group: 1645
Confirmation No.: 5474
Application No.: 09/821,726
Invention: GASTROKINES AND DERIVED
PEPTIDES INCLUDING
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Applicant: Terence Martin *et al.*
Filed: March 29, 2001
Attorney
Docket: 21459/90913
Examiner: Daniel M. Sullivan

Certificate Under 37 CFR 1.8(a)

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Sullivan - Commissioner for Patents, P.O. Box 1450,
Alexandria, VA 22313-1450

on December 1, 2003.

Alice O. Martin

AMENDMENT AND RESPONSE TO EXAMINER'S COMMUNICATION.

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

This amendment and response is filed in response to the examiner's communication.

Amendments to the claims are reflected in the listing of claims, which begins on page 2
of this paper.

Remarks/Arguments begin on page 5 of this paper.

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

1. (Previously Amended) 1. A group of isolated ~~homologous~~ cellular growth stimulating proteins designated gastrokines, said proteins produced by gastric epithelial cells and ~~comprising~~ consisting of an amino acid ~~the amino acids in the~~ sequence VKEK/QKXXGKGPGGXPPK (SEQ ID NO: 1).

2. (Previously Amended) An isolated protein ~~having a sequence of amino acids consisting of an amino acid sequence~~ from positions 21 to 185 of the sequence as shown in FIG. 8 (SEQ ID NO: 18), said protein present in pig gastric epithelia in a processed form lacking the 20 amino acids which constitute a signal peptide sequence, ~~having 165 amino acids and an estimated molecular weight of approximately 18 kD as measured by polyacrylamide gel electrophoresis, said protein capable of being secreted.~~

3. (Previously Amended) ~~An isolated~~ A recombinant human protein comprising ~~amino acids in the~~ the amino acid sequence as in FIG. 3 (SEQ ID NO: 13).

4. (canceled)

5. (Previously Amended) A growth stimulating peptide derived from a protein consisting of an amino acid sequence VKEK/QKXXGKGPGGXPPK (SEQ ID NO: 1) ~~of claim 1.~~

6. (Previously Amended) A modified peptide produced by the method comprising the following steps:

- (a) eliminating major protease sites in an unmodified peptide consisting essentially of an amino acid sequence VKEK/QKXXGKGPGGXPPK (SEQ ID NO: 1) by amino acid substitution or deletion in the unmodified peptide ~~derived from a protein of claim 1;~~ and
- (b) optionally introducing amino acid analogs of amino acids or D-amino acids in the unmodified peptide to produce a modified protein.

7. (Original-allowed) A synthetic growth stimulating peptide, having a sequence of amino acids as in positions 78 to 119 of the sequence shown in FIG. 3 (SEQ ID NO: 13).

8. (Currently Amended) A synthetic growth stimulating peptide having consisting of a sequence of amino acids from position 97 to position 117 as shown in FIG. 3 (SEQ ID NO: 13)

9. (Currently-Amended) A synthetic growth stimulating peptide ~~having~~ consisting of a sequence of amino acids from position 97 to position 121 as shown in FIG. 3 (SEQ ID NO: 13).

10. (Currently-Amended) A synthetic growth stimulating peptide ~~having~~ consisting of a sequence of amino acids from position 104 to position 117 as shown in FIG. 3 (SEQ ID NO: 13).

11. (Original-allowed) An isolated bioactive peptide consisting of a sequence selected from the group consisting of LDTMVKEQKGKGGAPPKDLMY (SEQ ID NO: 2) and KKLQGKGGPPPK (SEQ ID NO: 3).

Claim 12 (Previously Withdrawn)

Claims 13-15 (Canceled)

Claims 16-21 (Previously Withdrawn)

Claim 22 (Canceled)

Claims 23-26 (Previously Withdrawn)

Claims 27-29 (Canceled)

30. (New) A synthetic growth stimulating peptide comprising an amino acid sequence from position 97 to position 121 as shown in FIG. 3 (SEQ ID NO: 13) and not asparagine at a position 72 amino acids toward the N terminal.

31. (New) A synthetic growth stimulating peptide comprising an amino acid sequence from position 97 to position 121 as shown in FIG. 3 (SEQ ID NO: 13) and not asparagine at a position 10 amino acids toward the N terminal.

32. (New) A synthetic growth stimulating peptide comprising an amino acid sequence from position 104 to position 117 as shown in FIG. 3 (SEQ ID NO: 13) and not asparagine at a position 79 amino acids toward the N terminal.

33. (New) A synthetic growth stimulating peptide comprising an amino acid sequence from position 104 to position 117 as shown in FIG. 3 (SEQ ID NO: 13) and not asparagine at a position 17 amino acids toward the N terminal.

34. (New) A synthetic growth stimulating peptide comprising an amino acid sequence from position 97 to 117 as shown in FIG. 3 (SEQ ID NO: 13) and not asparagine at a position 72 amino acids toward the N terminal.

35. (New) A synthetic growth stimulating peptide comprising a amino acid sequence from position 97 to 117 as shown in FIG. 3 (SEQ ID NO: 13) and not asparagine at a position 10 amino acids toward the N terminal.

REMARKS**I. Status of the Claims**

Claims 7-11 were allowed (Office Action mailed May 12, 2003).

Claims 9 and 10 are amended.

Claims 30-35 are added.

Claims 4, 13-15, 22, 27-29 are canceled reserving the right to prosecute in a continuing application.

Claims 12, 16-21, and 23-26 were previously withdrawn reserving the right to prosecute in a continuing application (restriction requirement).

Claims 1-3, 5-11, and 30-35 are pending.

II. Jacobs Does Not Anticipate Claims 8-10.

Amended claims 8-10 are in condition for allowance.

III. Claims 30-35

New claims 30-35 are based on claims 8-10 and refer to amino acid positions 25 and 87 in SEQ ID NO: 13. Applicants request allowance of claims 30-33.

IV. Other Issues.

FIG. 1A-1G and FIG. 4A-4G are amended to include SEQ ID NOS.

V. Summary and Conclusion

Applicants thank the examiner for helpful suggestions during the interview.

For the reasons stated above, applicants request allowance of all pending claims.

Please contact the applicants' representative if you have any questions.

No other fees are believed due at this time, however, please charge any additional deficiencies or credit any overpayments to deposit account number 12-0913 with reference to our attorney docket number (21459/90913).

Respectfully submitted,



Alice O. Martin
Registration No. 35,601

December 1, 2003



1/24

AGCTTTATAA CCATGTGATC CCATCTTATG GTTTC AATCC ATGCACAGGA

51 GGAAAATTGT GGGCACGAAG TTTCCAAAGG GAAAATTTAT AGATTGGTAG

101 TTAATGAAAT ACAGTTTTCC TCCTTGGCAA ATTTAATTTA CTAGCTTCAC

151 TGTATAGGAA AAAGCAGGAA AAAAATTAAA ACCAACTCAC CTCCAAACCT

201 GTTTTGAGCT TTTACTTGTC TGCCCAATTG ATAGTTTCTA CTCTCTGCTT

251 TTGATGAAAA TATTTTTTAT TATTTTAATG TAACTTCTGA AAATAAATT

301 ATCTAGAAGC AAATAAAAAG ATATTGCTTT TATAGTTCCC AGAAGGAAAA

351 AACAAACACT AGGAAAGTTC TATCTATCAG ATGGGGGAGA TGTGATGGAG

401 GCAGTGATAT TTGAGCTGAG CCTTGAACAA TGAACAGGAG TCTACCAAGC

451 GAGAGGCTAG CGGGTGGCCC TCAAGATAAA ACAACAGCAT GTACAAAGGC

501 ATGGAGACAT ACACATCTTG ACTCTTCAG GAATGGTGGG AACGCTGGTG

551 GAGCTAGAAT GTAGGTACAT AGCATAAAGT GGCAGACGGG AAGCCTTTGG

601 AAATCTTATT ACATAGGACC CTGGATGCCA TTCCAATGAC TTTGAATTTT

651 CTGTAGGCTG CCAGCGAAAT TTCCAAGCGT GATAGAGTCA TGTCTATCTA

701 TGCACTTCAG AAAGACAACC TCAGGGTTAA TGAAGAAAAT GCATTGGAAT

751 ATAAGAACT GGTGACCAGA GTGATCAATT GCATGACTGT TGTGAAAGTC

801 CAGGTGAGGG GAGCTGTGGG CAAGGTCAGA GTTGAGAGGC ATTTAGAGA

851 TAAAATGACA GTAACATAAGT AGATGTCAGG CTGAGAAGAA AGGGCTGTAC

901 CAGATATATG GTGCTATCAT TAAGTGAGCT CAACATTGCA GAAAAGGGGT

951 AGGTTTGGTG GGAGTTGCTC ACAAACATG TTTAGTCTAA GCAAACCAT

1001 TGCCATGGGC TCAGATAAAA GTTAAGAAGT GGAAACCATT CCTACATTCC

1051 TATAGGAGCT GCTATCTGGA AGGCCTAGTA TACACGTGGC TTTTCAGCTG

1101 TGATTTTGTT TGATTTTAGG GATTATTCTT TTTCTGAATC TGAGCAATGT

FIG. 1A

1151 TAGCGTGTA AATACTCACA CCCACAGCTT TGACTGGGTG AGAAGTTATC
1201 ATAAATCATA TTGAGTTTGT TGTGATACCT TCAGCTTCAA CAAGTGATGA
1251 GTCAGGTCAA CTCCATGTGA AAGTTCCTTG CTAAGCATGC AGATATTCTG
1301 AAAGGTTTCC TGGTACACTG GCTCATGGCA CAGATAGGAG AAATTGAGGA
1351 AGGTAAGTCT TTGACCCAC CTGATAACAC CTAGTTTGAG TCAACCTGGT
1401 TAAGTACAAA TATGAGAAGG CTTCTCATTC AGGTCCATGC TTGCCTACTC
1451 CTCTGTCCAC TGCTTTCGTG AAGACAAGAT GAAGTTCACA GTGAGTAGAT
1501 TTTTCCTTTT GAATTTACCA CCAAATGATT GGAGACTGTC AATATTCTGA
1551 GATTTAGGAG GTTTGCTTCT TATGGCCCCA TCATGGAAAG TTTGTTTTAA
1601 AAAAATTCTC TCTTCAAACA CATGGACACA GAGAGGGGAA CAACACACAC
1651 CAGGTCCTGT TGGGGGGTGG AGAGTGAGGG GAGGGAACTT AGAGGACAGG
1701 TCAATAGGGG CAGCAAACCA CCATGGCACA CATATACCTA TGTAACAAAC
1751 CTGCACGTTT TGCACATGTA TCCCTTTTTT TTAGAAGAAG AAATAATGAA
1801 AAAAAACCTT TTTTCTATTT ATATAATCAT GGCATTTATA AGCATCTCTA
1851 TAGAGAAGGA TAATTGTGCT GAGATTAGAC AGCTGTCTGA GCACCTCACA
1901 CTGACCTATT TTTAACAAAA TGACTTTCCA CATCACCTGA TTTCGGCTCC
1951 ATGCRGGGTA AGCAGTTCCT AAGCCCTAGA AAGTGCCGAT CATCCCTCAT
2001 TCTTGAATTC CTCCTTTTAT TTACCAAAAT TCCTGAGCAT GTTCAGGAAA
2051 GATGAAAAGC TTATTATCAA AATAAGTGGC TGAGATAGAC TTCTTGTCAC
2101 ATTTGTTACA GTAAAATGGG TCTCCAAGAA AGAAAGATTT GCCTTGGGCT
2151 CTAGCATGGC CATTTATTTA AGAAAGCATC TGAAACATGA AGCTACCACA
2201 GCATCTCTCC TGTGGTTCCA GACGGAAGCC TGAGAGTCTA GGAGGAGGTG
2251 GACCGAGAAA CCCTGCCAAA GTAAC TAGTA GTGCCGGGTT TCTCACAACA

FIG. 1B

2301 CGATGCAAAG GGGCTAGAAT CAGATGACTA TTTTCATGTT TCAACATACT
2351 ACACACTGGA AAACGTTACG GCAGACTCTA CTTTATAATG GGGCTGCAAA
2401 TGTA AAAATGA CTACTAGAAC TAGGTCCTCT TAATAGCAGC AAAGTTTAAA
2451 AGGGTCAGAG GGAGCTCCAG ACACAGGTTA GATTTGATTT CTCTCCTAGT
2501 TCTGCTGTGA ACAAGAGGTA TAAGTTTGGC CAACTCACTT AACCCCTGAA
2551 GCTCAGTTAC CTTATCTGTA AAATGATTGC ATTGTACTAG GTGTTCTCTA
2601 AAATTTCTTC TACCTCTGAC TTTT TAGGAG ACTAATTTTT AACTCCTTTT
2651 TAAGCTATTG GGAGAAAAAT TTAATTTTTT TTCAAAAGTT ACCTTGAATC
2701 TCTAGAGCAG TTCTCAAAAC TATTTTGTCC CAGGCAAAGG AAATGAGACT
2751 AGGTACCCAG AATGAGGCAC CCTGCATAAA GCTCTGTGCT CTGAAAACCA
2801 ATGTCAGGGA CCCTGTGATA AATAATTAAA CCAAGTATCC TGGGACACTG
2851 CTAGTGACAT CGCCTCTGCT GATCACTCTT GCCAGCGAGA CACTCTATAC
2901 TTGCTTTCTC ATCATTGGCA TCCAAACTGC CTACTAATCC ATTGCTTTGG
2951 AAAGTTTTTT TTAATAAAAA GATTATTTCT ATTAGGAGGA AAACATCCCA
3001 TGTTAAATAG GAAAATTAAC TGAAATCATT TTCAGATGTG ATTTT TAGCA
3051 CTTATAGCCA TTTCAAACCA TGGTATTCAT TTATACTATG CTATTTATTG
3101 TAAAACTTCT TTTTTTTTCC AAGGAAAATA AGATAGTTTG CTTTATTTTA
3151 AAACAGTAAC TTTCTTATAT TGGGGCACTG ACCAAAATTC AATACTGGTA
3201 CAAATATGTT ACCTAGGGGG TCAAAATATG TGCCAGGTGA ATTTTCTGAA
3251 TTTCTCTAAA GAGAGAATTT TAAACCTTAT AAAACAATTA GAAACAAGTG
3301 AGTGAGAGGT GAGCATCAAC AACCTGTGTA ACATAAGCCA CAGTACAAAT
3351 TTAAGCTGAA TAACCAAGCC ATGTCAGTTA TCCCAAATCA TTTTGTGTTAA
3401 TATTTAGGAG GATACACATA TTTTCAATAA CTTAAAAGTG AATCTTTACT
3451 CCTATCTCTT AATACTCGAA GAAGTATAAC TTTCTTCTTT TACTAGATTT

FIG. 1C

3501 AAATAATCCA AATATCTACT CAAGGTAGGA TGCTGTCATT AACTATAGCT
 3551 GAGTTTATCC AAAATAGAAA AATCATGAAG ATTTATAAAG CATTTTAAAA
 3601 ATAATCATTT ATAGCAAGTC CTTGAAAGCT CTAAATAAGA AAGGCAGTTC
 3651 TCTACTTTCT AATAACACCT ATGGTTTATA TTACATAATA TAATTCAACA
 3701 AACACGCATT CTGACCAATG ATAATTTATA GGAAATTCAT TTGCCAAGTA
 3751 TATGTTTTAT TATAAAGTTA ATATTTTGAC CAATCTTAAA AATTTTTTAAA
 3801 CTCTATTCTG ACATTTCCAG AAGTATTATC TTAGCAAGTC ATCTTTATGA
 3851 TACCACTTAT TAAACTGAAG AGAAACAAGA TGGTACATTC TGGGTTTTAC
 3901 TTTAAAAGGG ATTTGATTCA ATAATTTGAT TTATCACTAC TTGAAAATTA
 3951 CATTTTCTTC CTCAGACTGG ATGGCAATGA GATGAAAGCA GCTTTCCTGG
 4001 CTCTCAACTT CCCTTCTTCA TCAATTTTTC CAGCGTTTCA TAAGGCCTAC
 4051 ACTAAAAATT CTAAACTAT ATATCACATT AATATAATTA CTTATAATTA
 4101 ATCAGCAATT TCACATTATC GTTAAAACCT TTATGGTTAA AAAATGCAAG
 4151 GTAAGAGAAG AAAAAACAC ATTGAACTAG AACTGAACAC ATTGGTAAAA
 4201 TTAGTGAATA CTTTTATAA GCTTGGATAG AGGAAGAAAG AAGACATCAT
 4251 TTTGCCATGT AACAGGAGAC CAATGTTATT TGTGATTTCA GATTGTCTTT
 4301 GCTGGACTTC TTGGAGTCTT TCTAGCTCCT GCCCTAGCTA ACTATGTAAG
 4351 TCTCACCTTT TCAAGTTTGC TACCAAAATG CATTTGCAAG GAAATGTGAT
 4401 ATTAAATCAC TCTCAATCTC TTATAAACTT CAGAATATCA ACGTCAATGA
 4451 TGACAACAAC AATGCTGGAA GTGGGCAGCA GTCAGTGAGT GTCAACAATG
 4501 AACACAATGT GGCCAATGTT GACAATAACA ACGGATGGGA CTCCTGGAAT
 4551 TCCATCTGGG ATTATGGAAA TGTAGGTAGT CAACGTGCAA TTTTCACTTT
 4601 ATTGTTTAAA AATACGACTT CTTTTTAACA AAAAATGTGC ATGTTAACCA
 4651 TAAAGAAATT AAAAATAAAT TCTAATTACA CATAGCATAC AGTTATAAGT

FIG. 1D

4701 AAAGGTGACC ATTTTGCTCA TCCGATTTTG TTCCCTAGAG ATAACACTG
4751 TTAATAAGTG TTGCATGATC AGTTAAAATT CAAACCAACA AACACTATGT
4801 TCAAGGGATT GTGGGTATAT ACAACAAATA TGAACATCCT TTTGCCTTGC
4851 CTGCAGATAC CCTCAATAAT GCTGAAAGAC TTATACAACA TTAGTGCTTC
4901 CAAAGCTTAG ACTATCTCAC TTTGTTTTCA AAGGAGGTTT TACGACCTTC
4951 TAAAGAGATT GAAATTGACA TTTCACCTAA AACTCGGGAA ATGTAAATGA
5001 CAATATTAAT TGGTAAGAGA GGAAAGAAGA AAGAAAGAAG GAAGGAAAGA
5051 AAGAAAGAAG GAAGGAAGGA AAGAAAGAAA GAAAGAAAGA AAGAGAGAGA
5101 AAGAAAGAAA AAGAAAAAAG AGAGAAAGAG AGAAGGAAAG AAAGAGAGAA
5151 GGAAAGGAAA AGAGAAGCAA AGAAAGAGAG GAGCAAAGAA AGGAACACTT
5201 AGCACTAGTT GGGAGACCCA ACTCTGGAAT TATCAGCTAT ATATTTAACA
5251 AACGTTATAC TTTTAAATAG CAAACTCTTT ATTGTTTCAA TTTTATCTGG
5301 TCAATTGGAA AAATAATTTT TGTCTTATCT GTCTCCTTGA AATGTGAGGA
5351 TCAAAGGAGA CTAAAACATG ATAGCTTTTA AAGTCTATTT CAGTAAAACA
5401 GACTTATATA GAGGGGTTTT TATCATGCTG GAACCTGGAA ATAAAGCAAA
5451 CCAGTTAGAT GCTCAGTCTC TGCCCTCACA GAATTGCAGT CTGTCCCCAC
5501 AAATGTCAGC AATAGATATG ATTGCCAAGC AGTGCCCCAT CCAGTGCTCT
5551 TATCCCAGCT CATCACGATC TTGGAGTTCC CATTTCTCTC TGCAGGTGGA
5601 ACTGACCTCT GATAAGAAAA GCTCCTCGGA GAACACATGC CTCACTATTT
5651 GCCATCTACT TTAACAGGGC TTTGCTGCAA CCAGACTCTT TCAAAAGAAG
5701 ACATGCATTG TGCACAAAAT GAACAAGGAA GTCATGCCCT CCATTCAATC
5751 CCTTGATGCA CTGGTCAAGG AAAAGAAGGT AAAAATAAAA GGCTTTTTAT
5801 TTTTGGTGAG GGGAGAGGTT TTACATCCTT CAGTAAATAA CGAGAAGATC
5851 ACAGTCATTC CCTCTTGACT ACAGTATGTT GTAGTGTGCA GCACAAAGGG

FIG. 1E

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5901 GGAAGTTATT GGTGATTGCC TGAGGGAAGG CAACTTCTGC CACATCAAAT
5951 GCTGTGGCTC ACACCTACCT CTACAACCGC TGAGCAAAGC ACTTGAAACC
6001 TTGACTGTTA GAGGAGCAAA GCTCTGGTCA CACCAATAGG AGCCTCAGTA
6051 CTTTGCCAAG GACATTTTTTC TGCAAGAGTT AGTTAGGGTT ATTAGATTTA
6101 GCAAATGAAA ATAGAAGATA TCCAGTTAGG TTTGAATTTT AGGTAAGCAG
6151 CAGGTCTTTT TAGTATAATA TATCCTATGC AATATTTGGG ATATACTAAA
6201 AAAAGATCCA TTGTTATCTG AAATTCAAAT GTAAGTGGT ATTGTATATT
6251 TTGTCTGGCC ATACTAATCC AGGTGAGTGG AAAGAAGAGA TCCATAATGT
6301 TTTAAAATAT TTGCCTGAGT TCATATTCCT ATAAGTATA AATGAGTACC
6351 TTTCAATGAC AAGGTAGAGA AAATAAATAA ACTGCATTCT CAGAAGATGA
6401 TTATTACATA GTCTAATCCA AGGAATCTAT GATGACCAA TGAGGTCCAA
6451 GTTGCAGAAT AAATTAAGCC TCAGACTTCT GTGTTTATGA GAAGCTGAGG
6501 TTTCAAACCA GGTAAATCCC TTAGGACACT TAGAAATGCT AAGATATACA
6551 GAATAAGCTA GAAATGGCTC TTCTTCATCT TGATTATGGA AAAATTTAGC
6601 TGAGCAACAC TCACTGTTGG CCTCGTATAC CCCTCAAGTC AACAAACCAC
6651 TGGGCTTGGC ATTCATTCTC TCCCATTCTT CCTTTCTACC TCTCTTTTCC
6701 AACTCAGCT TCAGGGTAAG GGACCAGGAG GACCACCTCC CAAGGGCCTG
6751 ATGTACTCAG TCAACCCAAA CAAAGTCGAT GACCTGAGCA AGTTCGAAA
6801 AACATTGCA AACATGTGTC GTGGGATTCC AACATACATG GCTGAGGAGA
6851 TGCAAGGTGA GTAGCATCCC TACTGTGCAC CCAAGTTAG TGCTGGTGGG
6901 ATTGTCAGAC TATCCTCGCG CGTGTCCATA GTGGGCACCA GTGATGCAGG
6951 GATGGTCATC AAGGCCAACA TTTGTGCAGT GCTTGCTCTG TGCCAGGTAC
7001 TGTTCTATGT GCTTTAAGTG TGTTAACTCG GTTCTTCACA GCAATCTTAT
7051 AGGTTCTATT TTAATCCTAC TTTATGGATG AGGAACTGA GGTACAGAGA

FIG. 1F

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7101 GGTCACAAAA TCCTTGCCTG GGTCAATTCC AAGCATTTTG GCTGTGGATT
7151 CTGTGCTCTT AAATATTATG GAACACTGCC TTTTAAGTGT GAATCAAGAG
7201 TAGACTCAAG TCATATTCAA AAGAATGCAT GAATGGCTAA ATGAAAGAAG
7251 AATGCTAATA GAATCTATTA ACTTTCTATA GCTCAGACAA TCACTTAATT
7301 TCTGGACATT CAAAGAACAG CTGCACACAA ACAAAGTGTC TACCTAGGGA
7351 CCTAACTTAA TGGCAATTTT CCAGATCTCT GAATTGATTG ATTTTCATCAC
7401 AACAAGTAGA TAAACCTTGA CATTAGCACA TAGCTAGTTT GGAAACCCCT
7451 ACTCCCCCAA TCCCCTCCAA GAAAAGAGTC CTAAATAGA CATTAATATA
7501 GGCTTCTTCT TTTCTCTTTA TTAGAGGCAA GCCTGTTTTT TTA CTAGGA
7551 ACGTGCTACA CGACCAGTGT ACTATGGATT GTGGACATTT CCTTCTGTGG
7601 AGACACGGTG GAGAACTAAA CAATTTTTTA AAGCCACTAT GGATTTAGTC
7651 ATCTGAATAT GCTGTGCAGA AAAAATATGG GCTCCAGTGG TTTTACCAT
7701 GTCATTCTGA AATTTTTCTC TACTAGTTAT GTTTGATTTC TTTAAGTTTC
7751 AATAAAATCA TTTAGCATTG AATTCAGTGT ATACTCACAT TTCTTACAAT
7801 TTCTTATGAC TTGGAATGCA CAGGATCAAA AATGCAATGT GGTGGTGGCA
7851 AGTTGTTGAA GTGCATTAGA CTCAACTGCT AGCCTATATT CAAGACCTGT
7901 CTCCTGTAAA GAACCCCTTC AGGTGCTTCA GACACCACTA ACCACAACCC
7951 TGGGAATGGT TCCAATACTC TCCTACTCCT CTGTCCACTG CTAA (SEQ ID NO: 11)

FIG. 1G

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1 GAATTCAAAC AGCAGGCCAT CTTTCACCAG CACTATCCGA ATCTAGCCAT
51 ACCAGCATTC TAGAAGAGAT GCAGGCAGTG AGCTAAGCAT CAGACCCCTG
101 CAGCCCTGTA AGCTCCAGAC CATGGAGAAG AGGAAGGTTG TGGGTTCAAG
151 GAGCTTTTCA GAGTGGAAAT CTGTGGATCA GTGATTTATA AAACACAGTT
201 TCCCCCTTTA TTAGATTTGA ACCACCAGCT TCAGTTGTAG AAGAGAACAG
251 GTTAAAAAAT AATAAGTGTC AGTCAGTTCT CCTTCAAAAC TATTTTAAAC
301 GTTTACTTAT TTTGCCAAGT GACAGTCTCT GCTTCCTCTC CTAGGAGAAG
351 TCTTCCCTTA TTTTAATATA ATATTTGAAA GTTTTCATTA TCTAGAGCAG
401 TGGTTCTCAT CCTGTGGGCC ATGAGCCCTT TGGGGGGGTT GAACGACCCT
451 TTCACAGGGG TCACATATCA GATATCCTGC ATCTTAGCTA TTTACATTAT
501 GATTCATAAC AGTAGCAAAA TTAGTTAGGA AGTAGGAACA AAATAACGTT
551 ATGGTTGTGG TCACCACTAT GTTAGAGGGT CCGCAGCATT CAGAGGGTTG
601 AGAACTGTTG TTCTAGAGGC AAATAAGAAG ACAGAGTTCC TTGATAGGGC
651 CCAGAGGCAG TGAAAGAAGT TTCCACGTAG AAAGTGAAGA AGGTCTGGTG
701 TCCGAAGCAG TGAGGAACTT AAAAAAGAA AACCAAAAAC ATTGCCAACT
751 AACAGTCCAG GAGAAGAGCG GGGCATGAAA GGCTGAGTTC CCATGGGATG
801 CCTTGAATGG AATCAGAGTG TGGGAAAATT GGTGTGGCTG GAAGGCAGGT
851 GCCGGGCATC TCAGACGCTG GTAGCTGGGG AAACAGGAAA CCCCTTTAGG
901 ATCCCAAGAT GCCATTCAA TGAGCTTGAG ATTTTCTCA TGGACTGCCA
951 GTGAATGTTT CTACGCTCCG GAAATTAATG TTTACTTATT TTCCATATTC
1001 TAGGGGAGAA CCCTGGGAAA AATGGAGGAC ATTCATTGAA ATATCTGAGT
1051 CCTGGGATAA GGCAGGCTTG GTCCTACAAC TCTGGTAAAA GTCCATCAGG
1101 AAGTGCCTTG ACCAAGGCTG GAGTGGAGAG CTGTTGGTGA GATGTAAGGG

FIG. 4A

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1151 CAAGGTTTAG TTGCTAGATA TGTAGATGGC AAGATGGTGC TGCCAACAGC
1201 CCCCAGAGCT CTAACCCACT GAGAAACCCA GGAATGAATG ATGGGAGATG
1251 GCTTTGGTGC CAGCTGCTAG TGACATGGCT GGAAAGCTGC ACTGGCTTCG
1301 AGGCCAGACA ATTCCTCAAG GAAACATCTG GCCAGGGTGC AAGGGCCAGT
1351 TTCCTTCCTT GGAGTTCCTT TCACAGCTAA GAACATCATC CCCCACCAC
1401 TGGTTTTGTT AAAAAGTTTT CAGTATGACT TGAGCATGGT CAAGAAGCAT
1451 AGAGAGGGGG AAATAAGGGT GGAAGGAGCT GGAGAAAGCT TACAATAGGA
1501 CTGGGTAAAG GGAAGGAGAA GAAACCATTC CCGCATTCCT ATAGGAGCCA
1551 GTACCAGGAA GGGCAGGTGT ACACACAGAT CTCATCTAAG GCCATGTTTG
1601 GTTTAGGGAT TACTCTTCTC CCGAATCTGA GCAGCAGCAA TACGTAAAT
1651 ACCCACACCC ATGGCTTCCA TATTCCAGAA CTTATCACAA ACCGTGTAGA
1701 GTTTACTGAG ATACCTTCGT CAGAGGATGA GTCAGAGGCC TCCTGCCTAA
1751 GGGCCCTACT GAGCAGGCAG CTAAAGGCTT CCGGGCCTCT GCAGCTCCAC
1801 AGATACAGGA GAGGGAAGCA GATAAGCCGT GGACTCCACC TGAGCACACC
1851 TAGCTTGAGC AAAGCTGGTC AGGTACAAAT AGCAGAGGGC TGAATGTCTG
1901 TGAGCACGCC GCCTGATCCT CTGCTCCACC AACTCCTGC CGCCATGAAG
1951 CTCACAGTAA GTCAGATCTT CTTTTCAATG CAGCACCATA CAACATTAAT
2001 AGTCAGGGGT GAGGGGGTCT GACTCTTACG GCACTGTTAC CATAGTGGAA
2051 ATATTCTCCT TTCTTTTCAT GGAATCATGG TGTTTACAAG CATGTCCATA
2101 GAGAAGAAGA ATTGCCCCGG AAGAGCCTGT CACAGGCTGA ATACTGTAGA
2151 ATTGTCTTTC ACACCATCTG TTCCAAGGTT CTACTIONAAGA CGAGCAGTCT
2201 CTGGGCTCCA GAAAGAGTCT TTCTTAGCCT TGATCTCTTT CTTATTTCTG
2251 ATTTCTCCTT TCTTATCCAT GATTCCACT TTTACCAGTT CTGGGCATGT

FIG. 4B

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2301 TCCGGTCAGA CTGGAAGATC ACTGTTGTCA AAAC TAGTCT TCAACACTCT
2351 TGGCTGTTAA CATGAAAACA ACGGTCCTTG GGCCCTGTGC AAGCATTCTT
2401 TGGAGAAAGT CTCTGGGGAT GAAGCTATCT CAGTTTCCCC ACTGAAGTCC
2451 TAGGATACAG AGGCTCAAAC AGAGTGCACA TATTCAATTT CAGCATACTC
2501 TATTGGCGCT GCTTTATGAA TCATATGAAT TTATGGAATT GGAAATGTAA
2551 ACTATGACCA AGAAGCGTCC ACCTCAGAAC AGGTGGGGTG GGGAAGTCCA
2601 AGCACAGGCC AGAGGGCTGC GTTCTCTTTC TAGTCTGTGC TAGAGGAGTG
2651 GTTCTCGACC TTCCTAATGC TGTGACCCTT TAATACAGTT CCTCACGTTG
2701 TCGTGACTCC CAGCCATAAA ATTACTTTCA TTGCTACTGC ATAAGTGTAA
2751 TTTTGCTACC ATTATGAGTT GTAATGTAAA TATCTGATAT GCAAGATACC
2801 AGATAACCTA AGAAACGGTT GTTTGACCTT TAAAGGGGTC ACAACCCACA
2851 GGTGGAGAAC TACTGGTCTA GGGTCCTTTA CAGTCCTTTA GCTGCCTCAT
2901 TTACAGGAGA TAACATCATG CTCAAAAACT CCCTCCACAT TTGGCTTTTT
2951 GGGTTGTTTT GTTTTGTTTT TCAAGACAGG GTTCTCTGT GTAGCCCTGG
3001 CTGTCCTGGA ACTCACCTTT GTAGACCAGG CTGGCCTCGA ACTCAGAAAT
3051 CCGCCTGCTT CTGCCTCCTG AGCGCTGGGA TTAAAGGCGT GCGCCACCAT
3101 GTCTGGCTCA CATCTGGCTT TTTAAGAGAC CGATTTTAAC TTCTTGCAAT
3151 GAAAATAAAT ATAGTAGAAA TGCTTAACCT ACTAAGACAA TAAAAACAGG
3201 ATTCCTTCTG CTAGGAAGAA CACGTTCCAG ACTAAGGAAA AAAACCTTTT
3251 CAGGGCTTTC ATTACACTGT GCCATGCACT AATTTTATGT TTTCTTCATC
3301 AGTTTTCACT GTCTGAAATT CAGTGTCAAA ATTCTAAGAC TACATATGAA

FIG. 4C

3351 TATCATTACA GTAACCTCAGC AATTCTATGT TACCAGTAAG TTTTCTGTGA
3401 GTTTAAAAAA AAGGTGGAG AAGAAAGCAC AGATAGTTTA GCACATGGGT
3451 AAAATCAGTA ACTATTTCTG ATGAGCTTGG TGAAGATGCT GTAAACCATG
3501 CGACCACCAG TCCTGTTCTC TGTGCTTTCA GATGTTCGTC GTGGGTCTGC
3551 TTGGCCTCCT TGCAGCTCCT GGTTTGTCTT ACGTAAGTCT CATTTTCTG
3601 AAGTTCATTG TCAAACTGC ATTTACAGTG AAATGTGATC TTAAGTCACC
3651 CTCTGCTTCT TATGAACATT AGACGGTCAA CATCAATGGT AATGATGGCA
3701 ATGTAGACGG AAGTGGACAG CATTCGGTGA GCATCAATGG TGTGCACAAC
3751 GTGGCCAATA TCGACAACAA TAACGGCTGG GACTCCTGGA ATAGCCTCTG
3801 GGACTATGAA AACGTATGTA ATGGACACAC AGGGTAAAGA TATGGTGTAG
3851 CCACCACCCA TTAAAATTTT TGAGGTGAAT TCTAGCTGTT CATGAACATT
3901 AAAAGCTACC AGTAAAAGTG CCCATTCCAC TCAAAACAAT TTTACTTTTT
3951 TGCATATAAT TATTGCTAAT AAGTATTACA CAATAGGTCG AAATTCAAAG
4001 GGATCAATAG TAAGGATAAA AACTATGTAC AAAGACAAAC ACAGCATCCT
4051 TTGGTCTTCC CTGCAGAGAG TCTCCATGAT GTTAAAGGTC CAATGTTTTA
4101 TGGAGGCTGA ATGAAATACG AATGCCTCTG TGATGGAAAA GGCCCAACAT
4151 CTTATGGAGA ATGAGTGAAG TATGAATGCT ATTAGTTGTA AGAGAAGGCG
4201 ATGCAAAGCA ACACTTGGCA CCACCTGCCA ATTACTACTT TCCTATTTAA
4251 ATGTAGTTTA AAAAGCAAAG CCTGTCTTCC CTGCCTCCTG GAAACACTGC
4301 GGATGGAGGT AGACCAAGGT ATGACAGCCT TTAAAAGTTT GTCAGCAAAA
4351 CACTCCCCCA TACACACATA CACACACCCT CCTACTACAC TGGAAGTAA

FIG. 4D

4401 GCAAAGGCAG TGGGTTAGAT ATATCCACCC TCTAAGAGTT TGCAGGTCAT
4451 CTATATATGA TAGCCAGAGA CACAAC TGCA GGACAGCCAG ACTCTGAGCA
4501 CTCTCCCCAG CTCCTTGTAG CTCTGTTTCA GTGGTGACTT GTGACAAGAA
4551 TCCTGGGGAA CCTGTGCCTC ACTGTTCTCT GTCTTCTTTA ATAGAGTTTC
4601 GCTGCCACGA GACTCTTCTC CAAGAAGTCA TGCATTGTGC ACAGAATGAA
4651 CAAGGATGCC ATGCCCTCCC TTCAGGACCT CGATACAATG GTCAAGGAAC
4701 AGAAGGTAAA GTCCTGCCTT CTTCTTTGGA GTGACAGGAA GTCTTACAGT
4751 CTCCAGTACA CAGTGAAGTC ACCCCCATTG CCTCTTTGGT GGAGCATGAC
4801 AGCATGTTTG TCATGATAAA TGCCACAAAC ATGTAAACT GTTCAGTGTC
4851 TGCCTGAATG GAGGGTGGCT TCCACTGTGT CAGATGCCGT GGCCACATC
4901 TGCCTCTGCA GGGTCCAGTA AAGCACTGGC TATCTTGAGT GTCAGAGACC
4951 CAAAGGTCTG TACACTTCAG TACAAGCCCT CCATATTTCA AGGGCACACT
5001 CCTACAGTCG TTGGGGTTAT CAGAACTAGC AAACATAGAG ACTGGATTTT
5051 CAGATGAAAA GAAATCCTTT TTAAAGTCTA AGTATGCCTT ATACAATGTT
5101 TGAGATATTC TCAATACTAA AAAAAAAAAA ATTGTTGCTT GCTTGAAAAT
5151 CAAATGTAAC CAAGTGTCTT ATATCCAGTG TCAATCATGG CTGTAGTAGA
5201 TGGGAAGAGG GAGCCCGTGG TTTTCACAGT CAGACGCCTG AGTTATTCTT
5251 CTAAGTGATA AATTGGTTCC TATAACAAGC AAGCCAGTGA ATATAAATAA
5301 GCTCTATCTC AGAAGTTATC CTGTAGTGCT ACCCTAGAAT CTAAGAGAGC
5351 AAAAGTGCTT CAAATTTTCA AATAAGTTTT GCTTTGGACT TCTGTTTTTC
5401 TAAACAATA TAACTTCAAA CCATCTAAGC CTCGTGGGAC ACTTAGAAAT
5451 ACCAAGCCAT TCAAAGCTAG AATTGTTTCT TCACCTTACT TGAAAACAAA

FIG. 4E

5501 ATGACAACCA AAAATTGTCC CCACTGCCCT TGTACATCTT CAGATCAGTA
5551 AAGTCCTGGG CTCAGGGATC ATTCACCTTC TTTCTTTCCT TTCACACTCA
5601 ACTTCAGGGT AAAGGGCCTG GAGGAGCTCC TCCAAGGAC TTGATGTACT
5651 CCGTCAACCC TACCAGAGTG GAGGACCTGA ATACATTCGG ACCAAAGATT
5701 GCTGGCATGT GCAGGGGCAT CCCTACCTAT GTGGCCGAGG AGATTCCAGG
5751 TGTGTACCCT GAGATGCTGT ATATCCCAAT GCAGTACTGA GAGAGCCATC
5801 AGACACTCTA AAGTGTGACC ACAGACGGAC CAATCATGTG GATTATCAGA
5851 GCAAACACTT GCTTGCTCCT TGTCAGACAG TTGTCCATGC TTCAAAAGTT
5901 CATTAAAAAA AATAGTTCAC AGGCTCCTCA CAGAAACCTT AGTAGAATCC
5951 ACAGCTTCTG CTCTTAGTCT TACTTTTTAG AACTGAGAC CCAGAGAAAG
6001 GTCACAAAAC TTTTGTCTGG CTCAGGTTCT ATGTCTTTAA CTTTATAGAA
6051 TACCGTCTTT CTGGGTGGGT GGGCTCTAGA GTAAACTTCA AGTGAGTTCA
6101 AGGAAAGCAT GAGAAGTAGG GAAGACCAAA TGAAAGGAGA ATGCCAATGA
6151 AATCTATCGA TTCTATAGCG CCAATGCTTA ACTCCTAGGC GTTCAAAGAA
6201 TAGTATCCAC AAGGTGTCAG CCTAAGATCC TAATCTAACA GCAAGTTTTC
6251 AGATCTCTGA AGTGAAAAGA GAAAGCAAGA GAGGAACAGA GACAGAAACA
6301 GTAAGAGACA GAGAGGCAGA GACAAAGAGA CAGGGAGAAT AGAGAGGGAT
6351 TAAAATTAAT ATATAGTTTA GAAATTACGA CTCCTCACAG TCCCTGCAGA
6401 GTCCTAGGAT AGGCACTGAT TTGGACTTCT TTTCTTCTCA CTAGGACCAA
6451 ACCAGCCTTT GTACTCAAAG AAGTGCTACA CAGCTGACAT ACTCTGGATT
6501 CTGCGGATGT CCTTCTGTGG AACATCAGTG GAGACATACT AGAAGTCACA
6551 GGAAAACAAC CCGTGGGCTC TGACCATCGC AATGCTTGAT TATGAGAGTG

FIG. 4F

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6601 TTCTCTGGGG GTTGTGATTA GCTTCTTTAA GGCTCAATAA ACCCACGTGG
6651 CAGCACATCC AGTTTGTAAT GACATGCCTC ATGACTTCTA TGGGAGTCCA
6701 ATGTGGCACC TGCCAGCCTG TATTCAGGAC CTCTCCGCTA TAAAGCATCC
6751 CTCCAGAGTT TTCAAATACT ACAAAGCACA GCCTGGGTTT GGGCTCAGAT
6801 AGGCCACTGC TGCCTGACTA CATTACAGAC AAACAAGTTT TAAAAGAAAG
6851 AAAAAAGAGC TCAGAGTGGC TGAATCAGC AAGGGTGTTT TTCCTGCAAG
6901 GAGCCAGAAG TATCAATAAT CACCCAAGGA GGAGACACTG GGAATGAGAG
6951 ACTAGAACAC ACGCCTGCAG ATACGGAGAA CCTCAGCATT GCCGCTCTCT
7001 CCCATAACTG CACACCCCCT TCTGTAAACT CTGCTTCTTT CTTTCACCTG
7051 AAGATGGCCC TTGCTTTTTT TTATTATAGG ACANGATAAC TAGACCAGAA
7101 AGTCAACCTG ACTCTCTACA TTTATATGTC TTCCCAGNTC AAGAAATATT
7151 ATTTACTGGT GAATGGCACT TCTATATTCC CTTGGTTCAA TAAGTCTACA
7201 GGATCCATTC ATTGACAGGC CAAGAGTGAG ATCACATGAT ACCCAAGCAC
7251 ATGGGTCTTT CCTTGAAGGA GAAGGATCCA (SEQ ID NO: 14)

FIG. 4G